REMARKS

Claims 1 – 3, 23 – 25 and 50 - 51 are pending in the application. Claims 25, 50 – 51 have been cancelled as being drawn to non-elected subject matter. Claims 1, 2, 3 and 24 have been amended.

No new matter has been added by virtue of these amendments; support therefore can be found in throughout the specification and original claims of the application.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Objections

Claims 3 and 25 were objected to by the Examiner as reciting non-elected subject-matter. Applicant has re-written claims 3 and 25 to delete non-elected subject-matter. Applicant respectfully requests withdrawal of the objection.

Drawings

The Examiner argues that the drawings filed on 6/05/2005 are objected to under 37 CFR 1.83(a) because "they fail to show the specific details as disclosed in the brief description on pages 4 – 7 of the specification." (Office Action, p.2).

Applicants are preparing new drawings in compliance with 37 CFR 1.83(a) and will submit the drawings under separate cover.

Rejection of Claims 1 - 3 and 23 – 25 Under 35 USC 112, First Paragraph

The Examiner has indicated that claims 1 - 3 and 23 – 25 are rejected under 35 USC 112, first paragraph as, allegedly, failing to comply with the enablement requirement. The Examiner argues that the claims, while being enabling for a method of killing a tumor cell in vitro comprising contacting the cell in vitro with a small inhibitory RNA specific for a DNA repair protein and at least one DNA-damaging agent, does not

PAGE 6/10 * RCVD AT 4/8/2008 2:30:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-5/43 * DNIS:2738300 * CSID: * DURATION (mm-ss):02-46

reasonably provide enablement for a method of killing a tumor cell comprising contacting the cell in vivo with a siRNA specific for a DNA repair protein and at least one DNA-damaging agent. Applicants respectfully traverse this rejection.

The specification provides detailed teachings regarding the claimed methods. For example, throughout the specification Applicants provide teaching of adenoviral vectors for the expression of siRNA. Applicants direct the Examiner's attention, for example, to paragraphs [0113 – 0116] and Figure 5, which teach siRNA-encoding nucleic acid molecules that are contained within an adenoviral vector, which can be used to infect mammalian cells (e.g., human cells). Further, the specification at paragraph [0014] provides numerous references to techniques related to adenoviral infection, and the specification teaches methods of delivering adenoviral vectors to a cell. Applicants direct the Examiner to the specification, for example at paragraphs [0090 and 0091], which teach means of delivery of adenoviral vectors, carrier, multiplicity of infection, and dose of adenoviral vector to be used depending on conditions and particular vector.

The Examiner argues further that "the state of the prior art for in vivo applications using siRNA was unpredictable" (Office Action, p.6), and cites the Caplen et al. (Expert Opin. Bio. Ther. 2003) reference. The Examiner argues that "the key issues of delivering nucleic acids to the required tissues and cell type, while ensuring an appropriate level of efficacy with minimum toxicity induced by the vector system, have been problems the gene therapy field has struggled with for over a decade now." (Office Action, p.6)." Applicants disagree.

According to the MPEP at 2164. 05(a), "(t)he state of the prior art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains (and) the state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. Therefore, the state of the prior art must be evaluated for each application based on its filing date."

The field of adenoviral-based gene therapy was well-developed at the time the instant application was filed. Applicants direct the Examiner to paragraph [0114] of the published application, which list references published well before the filing date

detaining use of adenovirus in various techniques:

> For techniques related to adenovirus, see, inter alia, Felgner and Ringold (1989) Nature 337:387-388; Berkner and Sharp (1983) Nucleic Acids Res. 11:6003-6020; Graham (1984) EMBO J. 3:2917-2922; Bett et al. (1993) J. Virology 67:5911-5921; Bett et al. (1994) Proc. Natl. Acad. Sci. USA 91:8802-8806.

Further, the following publications: Int J Radiat Oncol Biol Phys. 2003 Jan 1;55(1):204-14; Cancer Res. 2001 Oct 15;61(20):7464-72; Cancer Res. 2001 Jul 15;61(14):5453-60, demonstrate the success of adenoviral gene therapy. Copies of these publications can be provided upon the Examiner's request.

Rejection of Claim 1 Under 35 USC 102(b)

The Examiner has rejected claim 1 under 35 USC 102(b) as being anticipated by Collis et al. (Nucleic Acids Research, Vol. 29, No. 7: 1534-1538). Applicants respectfully traverse the rejection.

Claim 1 recites a method of killing a tumor cell comprising contacting the cell with at least one small inhibitory RNA (siRNA), wherein the siRNA is encoded by a nucleic acid molecule that is at least 85% identical to SEQ ID NO: 4, or a portion thereof, specific for a DNA repair protein and at least one DNA-damaging agent.

To anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

The Collis reference does not teach or suggest all the limitations of the instant claims. In particular, the Collis reference does not teach or suggest contacting the cell with at least one small inhibitory RNA (siRNA), wherein the siRNA is encoded by SEQ ID NO: 4, specific for a DNA repair protein.

As pointed out by the Examiner, "Collis et al. teach a method of treating human prostate cancer cells LNCaP with a ribozyme molecule targeted to a gene encoding a RAD51 protein." (Office Action, p.10).

The Examiner argues that "(t)he instant specification does not define a siRNA structurally and discloses a small inhibitory RNA as being specific for a DNA repair protein and capable of decreasing expression of said DNA repair protein therefore...a small inhibitory RNA as claimed embraces any small RNA molecule capable of inhibiting expression of DNA repair protein." (Office Action, p.9 – 10).

First, Applicants submit that the instant specification provides clear teaching directed to the structure and function of siRNA. Moreover, siRNA and RNAi technology were known and well- described in the art at the time of filing. Applicants direct the Examiner to, for example, paragraph [0049] of the published application, which provides extensive background and references to siRNA and RNAi technology, describes the use of siRNA in attenuating gene expression, and describes siRNA as sequence-specific, double-stranded RNA molecules. In contrast, and as appreciated by the Examiner, ribozymes "comprise two single stranded oligonucleotides." (Office Action, p.10).

Second, nowhere does the Collis reference teach a nucleic acid molecule that is at least 85% identical to SEQ ID NO: 4, or a portion thereof.

Accordingly, the Collis reference does not teach the limitations of the instant claims. Applicants respectfully request that the rejection be withdrawn.

Rejection of Claim 1 Under 35 USC 103(a)

Claims 1 - 3 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Fan et al. (Cancer Gene Therapy 2000, Vol. 7, No. 10: 1307 – 1314), in view of Hammond et al. and Tuschl et al. (WO 02/44321). Applicants respectfully traverse the rejection.

Claim 1 was set forth above.

The Fan et al. reference fails to teach or suggest all the elements of the instant invention. In particular, the Fan reference does not teach or suggest contacting the cell with at least one small inhibitory RNA (siRNA), wherein the siRNA is encoded by a nucleic acid molecule that is at least 85% identical to SEQ ID NO: 4, or a portion thereof, specific for a DNA repair protein. Nowhere in the Fan reference is there any teaching or suggestion of SEQ ID NO:4.

Neither of the Hammond nor the Tuschl references cure the defects of the Tan reference. Nowhere in either of the Hammond or the Tuschl references is there teaching or suggestion of the specific sequence set forth as SEQ ID NO:4. Therefore, the teachings of the cited art, when combined, do not result in the claimed invention.

Accordingly, Applicants request that the rejection be withdrawn.

Early consideration and allowance of the application are earnestly solicited.

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Respectfully submitted,

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PAGE 10/10 * RCVD AT 4/8/2008 2:30:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-5/43 * DNIS:2738300 * CSID: * DURATION (mm-ss):02-46